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(FILE 'HOME' ENTERED AT 19:31:40 ON 23 OCT 2006)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH, LIFESCI' ENTERED AT 19:32:00 ON 23 OCT 2006

L1 0 S ALPHA2/DELTA1  
L2 211 S ALPHA-2(W)DELTA-1  
L3 214765 S TRANSGEN?(6A) (ANIMAL OR MAMMAL OR MOUSE OR MICE OR RAT ORRABB  
L4 5 S L2 AND L3  
L5 5 DUP REM L4 (0 DUPLICATES REMOVED)

=> d au ti so pi ab 1-5 l5

L5 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

IN Luo, Zhigang David

TI Use of a transgenic mouse overexpressing .

alpha.2.delta.1 subunit of  
voltage-gated calcium channel as a model for nociception, pain  
transduction, and screening for analgesic compounds

SO PCT Int. Appl., 42 pp.

CODEN: PIXXD2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006017293	A2	20060216	WO 2005-US24697	20050712
WO 2006017293	A3	20060629		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AB The alpha-2-delta-1 subunit of a voltage-gated calcium channel (Cav.alpha.2. delta.1) is preferentially over-expressed in a non-human transgenic mouse model for neuropathic pain. Such transgenic animals advantageously exhibit non-injurious tactile allodynia and/or thermal hyperalgesia while retaining normal pain reaction to tissue injury and inflammatory pain. Thus, and in significant contrast to heretofore known animal models for neuropathic pain that require injury to precipitate the neuropathic pain, response behavior of the animal to a stimulus can be clearly attributed to the over-expression of the Cav.alpha.2.delta.1 subunit. The data presented strongly support that elevated Cav.alpha.2. delta.1 subunit is a mol. determinant of certain types of neuropathic pain. The results of the present study suggest that blocking pathways related to Cav.alpha.2. delta.1 subunit induction post peripheral nerve injury or the effects of elevated Cav.alpha.2. delta.1 subunit on VGCC may enable the development of compds. that act on both peripheral and central VGCC specifically involved in neuropathic pain expression.

L5 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

AU Li, Chun-Ying; Zhang, Xiu-Lin; Matthews, Elizabeth A.; Li, Kang-Wu; Kurwa, Ambereen; Boroujerdi, Amin; Gross, Jimmy; Gold, Michael S.; Dickenson, Anthony H.; Feng, Guoping; Luo, Z. David

TI Calcium channel .alpha.2.delta.1 subunit mediates spinal hyperexcitability in pain modulation  
 SO Pain (2006), 125(1-2), 20-34  
 CODEN: PAINDB; ISSN: 0304-3959  
 AB Mechanisms of chronic pain, including neuropathic pain, are poorly understood. Upregulation of voltage-gated calcium channel (VGCC) .alpha.2.delta.1 subunit (Cav.alpha.2.delta.1) in sensory neurons and dorsal spinal cord by peripheral nerve injury has been suggested to contribute to neuropathic pain. To investigate the mechanisms without the influence of other injury factors, we have created transgenic mice that constitutively overexpress Cav.alpha.2.delta.1 in neuronal tissues. Cav.alpha.2.delta.1 overexpression resulted in enhanced currents, altered kinetics and voltage-dependence of VGCC activation in sensory neurons; exaggerated and prolonged dorsal horn neuronal responses to mech. and thermal stimulations at the periphery; and pain behaviors. However, the transgenic mice showed normal dorsal horn neuronal responses to windup stimulation, and behavioral responses to tissue-injury/inflammatory stimuli. The pain behaviors in the transgenic mice had a pharmacol. profile suggesting a selective contribution of elevated Cav.alpha.2.delta.1 to the abnormal sensations, at least at the spinal cord level. In addition, gabapentin blocked VGCC currents concentration-dependently in transgenic, but not wild-type, sensory neurons. Thus, elevated neuronal Cav.alpha.2.delta.1 contributes to specific pain states through a mechanism mediated at least partially by enhanced VGCC activity in sensory neurons and hyperexcitability in dorsal horn neurons in response to peripheral stimulation. Modulation of enhanced VGCC activity by gabapentin may underlie at least partially its antihyperalgesic actions.

L5 ANSWER 3 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
 AU Li, Chun-Ying [Reprint Author]; Li, Kang-Wu; Kurwa, Ambereen; Feng, Guoping; Luo, Z. David  
 TI Characterization of injury free transgenic mouse showing neuropathic pain like behaviors.  
 SO FASEB Journal, (MAR 7 2005) Vol. 19, No. 5, Suppl. S, Part 2, pp. A1071. Meeting Info.: Experimental Biology 2005 Meeting/35th International Congress of Physiological Sciences. San Diego, CA, USA. March 31 -April 06, 2005. Amer Assoc Anatomists; Amer Assoc Immunologists; Amer Physiol Soc; Amer Soc Biochem & Mol Biol; Amer Soc Investigat Pathol; Amer Soc Nutr Sci; Amer Soc Pharmacol & Expt Therapeut; Int Union Physiol Sci. CODEN: FAJOEC. ISSN: 0892-6638.  
 AB Mechanisms underlying neuropathic pain are not clear. Previous studies have suggested that increased voltage-gated calcium-channel alpha(2)delta(1) (Ca(v)alpha(2)delta(1)) subunit in spinal cord and dorsal root ganglia (DRG) may contribute to neuropathic pain development/maintenance. To determine the causal role of Ca(v)alpha(2)delta(1) in neuropathic pain without complications from other injury factors, we generated and characterized transgenic mice overexpressing the Ca(v)alpha(2)delta(1) in neuronal tissues. Immunoblots showed elevated Ca(v)alpha(2)delta(1) expression in forebrain, hippocampus, cortex, cerebellum, spinal cord and DRG, but not in non-neuronal tissues. Compared with wild-type littermates, the transgenic mice showed reduced paw withdrawal threshold to mechanical stimulation and shortened paw withdrawal latencies to thermal stimulation, similar to neuropathic pain behaviors in nerve injured animals and patients. The hypersensitivity was reversed completely in a dose-related manner by gabapentin, an antihyperalgesic drug that binds to the Ca(v)alpha(2)delta(1), and partially by morphine. Ketorolac (COX

inhibitor) and ondansetron (5HT3 receptor antagonist) did not show any effect. These data support that increased  $Ca(v)\alpha(2)\delta(1)$  contributes to the development and maintenance of neuropathic pain like behaviors and this transgenic mouse can serve as a model for studying mechanisms of abnormal sensation and screening new antihyperalgesic agents.

L5 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN  
 IN Baron, Scott Phillip; Hidayetoglu, Debra Lynn; Johns, Margaret Ann; Offord, James David; Su, Ti-zhi  
 TI Non-human mammals and animal cells carrying mutations in the  $\alpha(2)\delta(1)$  voltage-sensitive calcium channel genes  
 SO PCT Int. Appl., 124 pp.  
 CODEN: PIXXD2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089072	A2	20041021	WO 2004-IB1187	20040405
WO 2004089072	A3	20041216		
WO 2004089072	C1	20050217		
WO 2004089072	C2	20051215		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1615493 A2 20060118 EP 2004-725751 20040405  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR  
 US 2005044581 A1 20050224 US 2004-823447 20040413  
 US 2005144659 A1 20050630 US 2004-823432 20040413

AB Transgenic animals carrying mutations in the genes for  $\alpha(1)$  subunit of the voltage-gated calcium channel in combination with mutations in the gene for the  $\delta(1)$  subunit are described. These animals carry mutations that abolish the binding of gabapentin and animals carrying them can be used to study the biol. role of voltage-gated calcium channels and in the development of novel drugs. Homozygous mutations in the  $\alpha(2)\delta(2)$  subunit gene are lethal in mice. Mutations in the  $\delta(1)$  locus led to altered response to pregabalin and in pain perception.

L5 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN  
 IN Baron, Scott Phillip; Hidayetoglu, Debra Lynn; Offord, James David; Su, Ti-zhi  
 TI Non-human mammals and animal cells carrying mutations in the  $\alpha(2)\delta(8)$  voltage-sensitive calcium channel genes  
 SO PCT Int. Appl., 176 pp.  
 CODEN: PIXXD2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089071	A1	20041021	WO 2004-IB1110	20040412

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,

BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,  
 ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,  
 SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,  
 TD, TG

EP 1615494	A1	20060118	EP 2004-726877	20040412
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2006522599	T2	20061005	JP 2006-506459	20040412
US 2005044581	A1	20050224	US 2004-823447	20040413
US 2005144659	A1	20050630	US 2004-823432	20040413

AB The invention relates features non-human mammals and animal cells that contain a targeted disruption of an  $\alpha$ .2/.  
 delta.1 and /or an  $\alpha$ 2/ $\delta$ 2 gene.

Transgenic animals carrying mutations in the genes for  $\alpha$ 1 subunit of the voltage-gated calcium channel in combination with mutations in the genes for the  $\delta$ 1 or  $\delta$ 2 subunits are described. These animals carry mutations that abolish the binding of gabapentin and animals carrying them can be used to study the biol. role of voltage-gated calcium channels and in the development of novel drugs. Homozygous mutations in the  $\alpha$ 2/ $\delta$ 2 subunit gene are lethal in mice. Mutations in the  $\delta$ 1 locus led to altered response to pregabalin and in pain perception.

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## Refine Search

### Search Results -

Terms	Documents
alpha- 2/delta-1	0

**Database:**

US Pre-Grant Publication Full-Text Database  
US Patents Full-Text Database  
US OCR Full-Text Database  
EPO Abstracts Database  
JPO Abstracts Database  
Derwent World Patents Index  
IBM Technical Disclosure Bulletins

**Search:**

L3

Refine Search

Recall Text

Clear

Interrupt

### Search History

DATE: Monday, October 23, 2006   [Purge Queries](#)   [Printable Copy](#)   [Create Case](#)

Set Name   Query  
side by side

Hit Count   Set Name  
result set

DB=PGPB,USPT; PLUR=YES; OP=AND

<u>L3</u>	alpha-2/delta-1	0	<u>L3</u>
<u>L2</u>	alpha2/delta1	0	<u>L2</u>
<u>L1</u>	alpha-2 adj delta-1	0	<u>L1</u>

END OF SEARCH HISTORY